PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants:	Alan D. Attie Donald L. Gillian-Daniel Paul W. Bates	Date: May 17, 2006
Serial No.:	09/620,820	Group Art Unit: 1636
Filed:	July 21, 2000	Examiner: Celine X. Qian
Title:	INHIBITION OF LIPOPROTEIN SECRETION	File No.: 960296.97290

SUPPLEMENTAL DECLARATION OF ALAN D. ATTIE

Commissioner For Patents
P. O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

I, Alan D. Attie, do hereby state and swear as follows:

1. I am the Alan D. Attie who is one of the inventors of this patent application, and I make this declaration in support of that patent application.

2. I am a professor in the Department of Biochemistry at the University of Wisconsin-Madison and all of the events described here arose out of work done in and with my laboratory at that institution.

3. I understand that the Patent Examiner is using a publication by Twisk et al. (*The Journal of Clinical Investigations*, Volume 105, Number 4, page 521, February 2000) to argue against the patentability of the claims of this patent application. I am familiar with this publication since it originated in my laboratory. I am one of the authors of the Twisk et al. paper, and I am the last listed author, which is the traditional listing for the author in whose laboratory the work was principally performed.

4. I also understand that the Twisk et al. paper is considered "by another" because the authors on the paper are different from the inventors listed on this patent application. The authors on the papers were those researchers who committed time, effort or resources to the research effort to determine whether or not deficiency in the LDL receptor was responsible for changes in VLDL secretions in individuals. Not all of the authors of the paper contributed to the concept which became the present invention. During the course of the research effort, Donald Gillian-Daniel and I saw that the insights discovered in the research described in the paper would enable us to design mechanisms to inhibit VLDL secretion in individuals. Those mechanisms are the methods and constructs described and claimed in this patent application. Donald Daniel-Gillen and I had already conceived and begun work on the inventions described and claimed in this patent application prior to the publication of the Twisk et al. paper in February 2000.

5. The authors of the Twisk et al. paper all did make research or resource contributions to the research work described in that paper. However, after careful consideration of the question, we believe the other authors on the Twisk et al. paper, other than Mr. Gillian-Daniel and myself, did not make inventive contributions to the subject matter claimed in this patent application. But to the extent that this patent application was taught or made obvious by the work described in this paper, it was Mr. Gillian-Daniel and myself, co-authors of that paper, who invented and conceived the fundamental invention in this patent application.

6. I also understand that the Examiner has expressed uncertainty about the contributions of Paul Bates, who is the other listed inventor on this patent application. As I indicated in my previous Declaration, Mr. Bates did much of the laboratory work described in this patent application. Mr. Bates was named as an inventor of the patent application because of his intellectual contribution to many of the details of the execution of this invention, some of which are encompassed by claims presently in the application. Specifically, Mr. Bates came up with the idea of reducing the invention to practice through use of a vector-based delivery system. This mode of delivery is described and exemplified in the application (see for example, pages 8-9 of the specification). However, nowhere in Twisk et al. does it contemplate or suggest delivering a genetic construct into the vein of a mammal to lower serum cholesterol. Thus, the

contributions of Mr. Bates particularly in regards to the gene delivery system described in the claimed invention are inventive over Twisk et al.

7. Specifically, I assert that Twisk et al. explores the relationship between the presence of the LDL receptor and lipoprotein secretion in hepatocytes from both wild-type and LDL receptor-deficient mice. Twisk et al. treats hepatocytes with recombinant adenoviruses to overexpress the LDL receptor in *Ldlr-/-* cells, resulting in degradation of approximately 90% of newly synthesized apoB100. (See Twisk et al., Abstract, pg. 524, col. 1; pg. 526, col. 2; Figs. 5 and 6). The differences between Twisk et al. and the claimed invention would readily be appreciated by one of ordinary skill in the art. In Twisk, *in vitro* experiments are conducted, where cells were treated with a genetic material in a controlled environment. In the present invention, *in vivo* experiments are conducted, where an inventive route of delivery was identified and effectively used for lowering serum cholesterol levels. Thus, the inventive contributions of Mr. Bates particularly in regards to the gene delivery system are not obvious and go well beyond the disclosure of the Twisk paper.

8. I hereby declare all statements made herein of my own knowledge are true and all statements made on information and belief are believed to be true; and further that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and the such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

A. Attie

Alan D. Attie

Date: 5/10/06